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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/091,912	03/05/2002	Richard R. Bott	GC724	9189

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GENENCOR INTERNATIONAL, INC.
ATTENTION: LEGAL DEPARTMENT
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EXAMINER	
STEADMAN, DAVID J	

ART UNIT	PAPER NUMBER
1656	

MAIL DATE	DELIVERY MODE
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/091,912	BOTT ET AL.	
	Examiner	Art Unit	
	David J. Steadman	1656	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 August 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,39-41 and 45-55* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,39-41 and 45-55* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *8/23/07*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of the Application

[1] Claims 1, 39-41, and 45-55 are pending in the application.

[2] Applicant's amendment to the claims, filed on 8/23/07, is acknowledged. This listing of the claims replaces all prior versions and listings of the claims.

[3] Receipt of an information disclosure statement, filed on 8/23/07, is acknowledged.

[4] Applicant's arguments filed on 8/23/07 in response to the non-final Office action mailed on 4/23/07 have been fully considered and are deemed to be persuasive to overcome some of the rejections and/or objections previously applied. Rejections and/or objections not reiterated from previous Office actions are hereby withdrawn.

[5] The text of those sections of Title 35 U.S. Code not included in the instant action can be found in a prior Office action.

Information Disclosure Statement

[6] All references cited in the information disclosure statement filed on 8/23/07 have been considered by the examiner. A copy of Form PTO-1449 is attached to the instant Office action. It is noted that US Patent 6,993,140 discloses a "3-N-1 Anti-Noise Radio Sound-Collection Device" and appears to be unrelated to the claimed subject matter.

Claim Rejections - 35 USC § 112, Second Paragraph

[7] Claims 1, 39-41, and 45-55 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1, 39 (claims 40-41 dependent therefrom), 45 (claims 46-52 dependent therefrom), and 53 (claims 54-55 dependent therefrom) are unclear in the recitation of "the amino acid sequence of said variant consists of substitutions of Met...of SEQ ID NO:2" (claim 1), "said variant consists of a substitution of Ile...of SEQ ID NO:2" (claim 39), "said variant consists of substitutions of Ala...of SEQ ID NO:2" (claim 45), and "said variant consists of a substitution of Leu...of SEQ ID NO:2". In this case, the "consists of...SEQ ID NO:2" phrases as noted above only specify the position of mutation relative to SEQ ID NO:2 and do not appear to limit the sequence of the variant itself. In view of the recitation of "consists of" with respect to the mutations, it appears applicant may intend for the sequence to be closed, *i.e.,* the sequence of the variant is closed and is SEQ ID NO:2, except the recited mutations. See particularly applicant's statement at p. p. 6, bottom of the instant remarks, "The 'consisting of' language in the claims as amended clarifies that the claimed cutinase variants are limited to specific substitutions within SEQ ID NO:2". However, MPEP 2111.01 states, "[d]uring examination, the claims must be interpreted as broadly as their terms reasonably allow." As such, the claims have been interpreted as the sequence of the variant is open-ended and can encompass any sequence of amino acids as long as it has mutation(s) relative to the positions of SEQ ID NO:2. In the interest of compact prosecution, it is noted that if applicant intends for the phrases to limit the sequence of the variant, it is suggested that

(using claim 1 as an example) the phrase "said variant consists of substitutions of Met...of SEQ ID NO:2" be amended to recite, "said variant consists of the amino acid sequence of SEQ ID NO:2, except for substitution of Met at position 192, Val at position 194, and Gly at position 219".

Claim Rejections - 35 USC § 112, First Paragraph

[8] The new matter rejection of claims 1, 19, 31, 34-41, 44, and 46-50 under 35 U.S.C. 112, first paragraph, (paragraph 10 beginning at p. 7 of the 4/23/07 Office action) is withdrawn upon further consideration of the rejection.

According to the holding in *Ex parte Parks*, 30 USPQ2d 1234 (Bd. Pat. App. & Int. 1993), "[i]n rejecting a claim under the first paragraph of 35 U.S.C. 112 for lack of adequate descriptive support, it is incumbent upon the examiner to establish that the originally-filed disclosure would not have reasonably conveyed to one having ordinary skill in the art that an appellant had possession of the now claimed subject matter. *Wang Laboratories, Inc. v. Toshiba Corp.*, 993 F.2d 858, 26 USPQ2d 1767 (Fed.Cir. 1993). Adequate description under the first paragraph of 35 U.S.C. 112 does not require *literal* support for the claimed invention. *In re Herschler,* 591 F.2d 693, 200 USPQ 711 (CCPA 1979); *In re Edwards,* 568 F.2d 1349, 196 USPQ 465 (CCPA 1978; *In re Wertheim,* 541 F.2d 257, 191 USPQ 90 (CCPA 1976). Rather, it is sufficient if the originally-filed disclosure would have conveyed to one having ordinary skill in the art that an appellant had possession of the concept of what is claimed. *In re Anderson,* 471 F.2d 1237, 176 USPQ 331 (CCPA 1973)." In view of the disclosure and original

claims, the instant specification would appear to provide adequate descriptive support for the claimed invention and the new matter rejection has been withdrawn.

[9] The written description rejection of claims 1, 39-41, and 45-50 under 35 U.S.C. 112, first paragraph, is maintained for the reasons of record and the reasons set forth below. The rejection was fully explained in a prior Office action (paragraph 11 beginning at p. 8 of the 4/23/07 Office action). Newly added claims 51-55 are included in this rejection. Thus, claims 1, 39-41, and 45-55 are rejected.

RESPONSE TO ARGUMENT: Applicant argues (instant remarks at p. 7, top) the rejection is obviated by amendment and that the claims as amended are directed to cutinase variants with specific mutations of an amino acid sequence "consisting of" SEQ ID NO:2.

Applicant's argument is not found persuasive. In this case, the amendment fails to overcome the written description rejection. As noted in prior Office actions, the basis for the rejection is the failure of the disclosed representative species to reflect the structural variation among the members of the genus. In this case, the "consisting of" language, which appears in the claim before the recited mutations – not the sequence of SEQ ID NO:2 - does not limit the sequence of the variant, only the recited mutations of the variant. As noted above, the claims have been interpreted as meaning the sequence of the variant is open-ended and can encompass any sequence of amino acids as long as it has mutation(s) relative to the positions of SEQ ID NO:2.

Consequently, the claims encompass widely variant species and for reasons of record, the disclosed species fail to be representative of the genus.

As further noted above, in the interest of compact prosecution, if applicant intends for the phrases to limit the sequence of the variant, it is suggested that (using claim 1 as an example) the phrase "...said variant consists of substitutions of Met...of SEQ ID NO:2..." be amended to recite, "...said variant consists of the amino acid sequence of SEQ ID NO:2, except for substitution of Met at position 192, Val at position 194, and Gly at position 219...".

It should be noted that the representative species of variants as disclosed in the specification appear to be variants of SEQ ID NO:2 *minus* a 14 amino acid leader sequence, *i.e.,* the mature form, not variants of SEQ ID NO:2 itself (see particularly pp. 16-17, Tables 2 and 3, respectively, of the instant specification). According to applicant, SEQ ID NO:2 is the mature form with an N-terminal 14 amino acid leader sequence (response filed on 7/15/04, p. 11, top). It is well-known that polypeptides with intact leader sequences are catalytically inactive, requiring cleavage to the mature form of the polypeptide for catalytic activity. As such, while the specification provides descriptive support for mutants of SEQ ID NO:2 (see, *e.g.,* original claim 1) and further shows possession of mutants of SEQ ID NO:2 *minus* a 14 amino acid leader sequence with increased polyesterase activity and/or thermostability relative to SEQ ID NO:2 *minus* a 14 amino acid leader sequence, there is no indication in the specification that applicant was in possession of variants of SEQ ID NO:2 *including* the 14 amino acid leader

sequence with increased polyesterase activity and/or thermostability relative to SEQ ID NO:2 *including* the 14 amino acid leader sequence.

[10] The scope of enablement rejection of claims 1, 39-41, and 45-50 under 35 U.S.C. 112, first paragraph, is maintained for the reasons of record and the reasons set forth below. The rejection was fully explained in a prior Office action (paragraph 12 beginning at p. 9 of the 4/23/07 Office action). Newly added claims 51-55 are included in this rejection. Thus, claims 1, 39-41, and 45-55 are rejected.

RESPONSE TO ARGUMENT: Applicant argues (instant remarks beginning at p. 7, bottom) the rejection is obviated by amendment and that the claims as amended are directed to cutinase variants with specific mutations of an amino acid sequence "consisting of" SEQ ID NO:2.

Applicant's argument is not found persuasive. In this case, the amendment fails to overcome the written description rejection. As noted in prior Office actions, the basis for the rejection is the failure of the disclosed representative species to reflect the structural variation among the members of the genus. In this case, the "consisting of" language, which appears in the claim before the recited mutations – not the sequence of SEQ ID NO:2 - does not limit the sequence of the variant, only the recited mutations of the variant. As noted above, the claims have been interpreted as meaning the sequence of the variant is open-ended and can encompass any sequence of amino acids as long as it has mutation(s) relative to the positions of SEQ ID NO:2. Consequently, for reasons of record, the specification's guidance and working examples

along with the knowledge of the prior art fail to enable all cutinase variants as encompassed by the claims without requiring undue experimentation.

As further noted above, in the interest of compact prosecution, if applicant intends for the phrases to limit the sequence of the variant, it is suggested that (using claim 1 as an example) the phrase "...said variant consists of substitutions of Met...of SEQ ID NO:2..." be amended to recite, "...said variant consists of the amino acid sequence of SEQ ID NO:2, except for substitution of Met at position 192, Val at position 194, and Gly at position 219...".

It should be noted that the working examples of variants as disclosed in the specification appear to be variants of SEQ ID NO:2 *minus* a 14 amino acid leader sequence, *i.e.,* the mature form, not variants of SEQ ID NO:2 itself (see particularly pp. 16-17, Tables 2 and 3, respectively, of the instant specification). According to applicant, SEQ ID NO:2 is the mature form with an N-terminal 14 amino acid leader sequence (response filed on 7/15/04, p. 11, top). It is well-known that polypeptides with intact leader sequences are catalytically inactive, requiring cleavage to the mature form of the polypeptide for catalytic activity. As such, while the specification provides descriptive support for mutants of SEQ ID NO:2 (see, *e.g.,* original claim 1) and further shows possession of mutants of SEQ ID NO:2 *minus* a 14 amino acid leader sequence with increased polyesterase activity and/or thermostability relative to SEQ ID NO:2 *minus* a 14 amino acid leader sequence, there is no indication in the specification that applicant was in possession of variants of SEQ ID NO:2 *including* the 14 amino acid leader

sequence with increased polyesterase activity and/or thermostability relative to SEQ ID NO:2 *including* the 14 amino acid leader sequence.

Claim Rejections - 35 USC § 103

[11] The rejection of claims 39 and 41 under 35 U.S.C. 103(a) as being unpatentable over Poulouse et al. (US Patent 5,352,594; "Poulouse") is maintained for the reasons of record and the reasons set forth below. The rejection was fully explained in a prior Office action (paragraph 13 beginning at p. 11 of the 4/23/07 Office action). In view of the instant amendment, claim 40 is included in this rejection. Also, newly added claims 53-55 are included in this rejection. Thus, claims 39-41 and 53-55 are rejected.

RESPONSE TO ARGUMENT: Applicant argues (instant remarks beginning at p. 8, bottom): 1) the Poulouse reference fails to provide a reasonable expectation of success for achieving a cutinase variant having the recited increased polyesterase activity or enhanced thermostability and 2) a large number of variants is encompassed by Poulouse's suggestion to modify amino acids within six residues of Ser126, Asp176, and His206 (as acknowledged by applicant, corresponding to amino acids 140, 190, and 220, respectively, of SEQ ID NO:2).

Applicant's argument is not found persuasive. Initially it is noted that applicant relies on Poulouse's teaching of altering 6 amino acids within positions Ser126, Asp176, and His206 (corresponding to amino acids 140, 190, and 220, respectively, of SEQ ID NO:2), Poulouse narrows the alteration(s) to within four amino acids of the catalytic amino acid (see particularly claim 4).

It is the examiner's position that variants as encompassed by the claims would have been obvious at the time of the invention and that such variants, by virtue of their amino acid sequence, would have had the recited increased polyesterase activity or enhanced thermostability. The examiner acknowledges the requirements for increased polyesterase activity or enhanced thermostability in the claims. However, the prior art need not *expressly* teach these limitations. As noted by MPEP 2112, "[t]he express, implicit, and inherent disclosures of a prior art reference may be relied upon in the rejection of claims under 35 U.S.C. 102 or 103." Although Poulouse does not teach the resulting effects of substitution(s) within 4 amino acids of positions 140, 190, and 220, the reference nonetheless appears to suggest making the recited substitutions. Also, while it is acknowledged that the claims require specific mutations at position 192 or 194, as noted in the prior Office action, Poulouse expressly suggests replacing each of the amino acids within 6 of the catalytic triad with the 19 other amino acids (column 6, lines 41-47). Thus, according to the teachings of Poulouse, a number of variants would be produced, which would necessarily encompass all position 192 and 194 variants, including the specifically recited variants. Because the structure, *i.e.*, amino acid sequence, of a polypeptide determines its function, those polypeptides having the specifically recited substitutions as produced according to Poulouse would necessarily possess the recited increased polyesterase activity or enhanced thermostability. Although Poulouse does not appear to suggest that such variants will have the recited increased polyesterase activity or enhanced thermostability, "the claiming of a...new function or unknown property which is inherently present in the prior art does not

necessarily make the claim patentable." See MPEP 2112. Moreover, while achieving all variants as suggested by Poulouse would require some experimentation, the reference is nonetheless enabling by virtue of disclosing methods of making polypeptide variants.

[12] The rejection of claims 45-46, 48, and 50 under 35 U.S.C. 103(a) as being unpatentable over Poulouse (*supra*) is maintained for the reasons of record and the reasons set forth below. The rejection was fully explained in a prior Office action (paragraph 14 beginning at p. 13 of the 4/23/07 Office action). In view of the instant amendment, claims 47 and 49 are included in this rejection. Also, newly added claims 51-52 are included in this rejection. Thus, claims 45-52 are rejected.

RESPONSE TO ARGUMENT: Applicant argues (instant remarks beginning at p. 10, top): 1) the Poulouse reference fails to teach any of the claimed variants; 2) the reference fails to provide a reasonable expectation of success for achieving a cutinase variant having the recited increased polyesterase activity or enhanced thermostability and 3) a large number of variants is encompassed by Poulouse's suggestion to modify amino acids within six residues of Ser126, Asp176, and His206 (as acknowledged by applicant, corresponding to amino acids 140, 190, and 220, respectively, of SEQ ID NO:2).

Applicant's argument is not found persuasive. The examiner acknowledges that Poulouse fails to expressly disclose a variant having the specified mutations. However, it is the examiner's position that variants as encompassed by the claims would have been obvious at the time of the invention and that such variants, by virtue of their amino

acid sequence, would have had the recited increased polyesterase activity or enhanced thermostability. As previously stated, the prior art need not *expressly* teach these limitations. As noted by MPEP 2112, "[t]he express, implicit, and inherent disclosures of a prior art reference may be relied upon in the rejection of claims under 35 U.S.C. 102 or 103." Although Poulouse does not teach the resulting effects of substitution(s) within 4 amino acids of positions 140, 190, and 220, the reference nonetheless appears to suggest making individual substitutions and additionally suggests making multiple substitutions to "optimize the results." As such, one of ordinary skill in the art would have been motivated to make all combinations of mutations within 4 amino acids of positions 140, 190, and 220, which would encompass the recited mutations. While it is acknowledged that the claims require *specific* amino acid mutations at position 194 and 219, as noted in the prior Office action, Poulouse expressly suggests replacing each of the amino acids within 4 of the catalytic triad with the 19 other amino acids (column 6, lines 41-47). Thus, according to the teachings of Poulouse, a number of variants would be produced, which would necessarily encompass all position 194 and 219 double mutants, including the specifically recited variants. Because the structure, *i.e.,* amino acid sequence, of a polypeptide determines its function, those polypeptides having the specifically recited substitutions as produced according to Poulouse would necessarily possess the recited increased polyesterase activity or enhanced thermostability. Although Poulouse does not appear to suggest that such variants will have the recited increased polyesterase activity or enhanced thermostability, "the claiming of a...new function or unknown property which is inherently present in the prior art does not

necessarily make the claim patentable." See MPEP 2112. Moreover, while achieving all variants as suggested by Poulouse would require some experimentation, the reference is nonetheless enabling by virtue of disclosing methods of making polypeptide variants.

[13] Claim(s) 1 is rejected under 35 U.S.C. 103(a) as being unpatentable over Poulouse (*supra*) in view of Schumann et al. (*Protein Sci* 2:1612-1620, 1993; "Schumann"), LoGrasso (*Biochemistry* 30:8463-8470, 1991; "LoGrasso"), and Cunningham et al. (*Prot Engineer* 1:319-325, 1987; "Cunningham"). Claim 1 is drawn to a variant of SEQ ID NO:2 having substitutions of Met at position 192, Val at position 194, and Gly at position 219, wherein the variant has increased polyesterase activity as compared to SEQ ID NO:2.

Poulouse teaches that it would be useful to modify *P. mendocina* cutinase in order to alter its perhydrolysis/hydrolysis ratio, kcat, and Km (column 2, lines 52-54). In order to do this, Poulouse suggests altering an amino acid within "about six amino acids on either side of a catalytic amino acid" of *P. mendocina* cutinase (column 5, lines 42-57). See also claim 4, which narrows the alteration(s) to within four amino acids of the catalytic amino acid. Poulouse identifies Ser126, Asp176, and His206 (as acknowledged by applicant, corresponding to amino acids 140, 190, and 220, respectively, of SEQ ID NO:2 herein) as the *P. mendocina* cutinase catalytic triad amino acids (column 7, lines 12-14). Poulouse suggests replacing each of the amino acids within 6 (or 4) of the catalytic triad with the 19 other amino acids to select for those that have the "best ratio or substrate specificity" (column 6, lines 41-47). Poulouse further

teaches that multiple substitutions within the six (or four) amino acids of the catalytic triad "can be done to optimize the results" (column 6, lines 47-49). Poulouse does not make a triple mutant of *P. mendocina* cutinase as encompassed by the claims.

At the time of the invention, it was well-known in the art that multiple mutations can achieve enhancements over single or double mutations. For example, Schumann teaches a triple mutant of a *P. putida* creatinase that has a specific activity greater than either wild-type, single mutants, or a double mutant (p. 1614, Table 1) and has enhanced thermal stability relative to wild-type, single mutants, or a double mutant, wherein the stability increments are additive (p. 1616, column 1 and Table 3). Also, LoGrasso teaches a triple mutant of human carbonic anhydrase III, wherein the catalytic constant 500-fold higher than wild type (p. 8463, abstract). Further, Cunningham teaches a triple mutant of subtilisin that is more alkaline stable than single or double mutants (p. 319, abstract).

Therefore, at the time of the invention, it would have been obvious to one of ordinary skill in the art to make all possible triple mutants within 4 amino acids of the catalytic triad of the *P. mendocina* lipase of Poulouse with any of the 19 other common amino acids, which would have encompassed the recited variants and by virtue of their having the same structures, *i.e.,* amino acid sequences, as the variants of claim 1, would have necessarily had increased polyesterase activity. One would have been motivated to make all triple mutants within 4 amino acids of the catalytic triad of *P. mendocina* lipase because of the specific guidance of Poulouse to make multiple substitutions within the four amino acids of the catalytic triad in order "to optimize the

results" as suggested by Poulouse, and because it was recognized in the prior art that multiple substitutions could achieve enhanced results that are greater than either single or double mutants as shown by Schumann, LoGrasso, and Cunningham. One would have a reasonable expectation of success for making all possible triple mutants within 4 amino acids of the catalytic triad of the *P. mendocina* lipase of Poulouse with any of the 19 other common amino acids because of the results of Poulouse. Therefore, claim 1, drawn to the triple mutant as described above, would have been obvious to one of ordinary skill in the art at the time of the invention.

RESPONSE TO ARGUMENT: Applicant argues (instant remarks beginning at p. 11, top): 1) the Poulouse reference fails to teach any of the claimed variants; 2) the reference fails to provide a reasonable expectation of success for achieving a cutinase variant having the recited increased polyesterase activity or enhanced thermostability and 3) a large number of variants is encompassed by Poulouse's suggestion to modify amino acids within six residues of Ser126, Asp176, and His206 (as acknowledged by applicant, corresponding to amino acids 140, 190, and 220, respectively, of SEQ ID NO:2).

Applicant's argument is not found persuasive. The examiner acknowledges that Poulouse fails to expressly disclose a variant having the specified mutations. However, it is the examiner's position that variants as encompassed by the claims would have been obvious at the time of the invention and that such variants, by virtue of their amino acid sequence, would have had the recited increased polyesterase activity. As

previously stated, the prior art need not *expressly* teach these limitations. As noted by MPEP 2112, "[t]he express, implicit, and inherent disclosures of a prior art reference may be relied upon in the rejection of claims under 35 U.S.C. 102 or 103." Although Poulouse does not teach the resulting effects of substitution(s) within 4 amino acids of positions 140, 190, and 220, the reference nonetheless appears to suggest making individual substitutions and additionally suggests making multiple substitutions to "optimize the results." Moreover, the prior art provides evidence that triple mutants can achieve desired results that are greater than either a single or double mutant. As such, one of ordinary skill in the art would have been motivated to make all combinations of triple mutations within 4 amino acids of positions 140, 190, and 220, which would encompass the recited mutations. While it is acknowledged that the claims require *specific* amino acid mutations at position 192, 194, and 219, as noted in the prior Office action, Poulouse expressly suggests replacing each of the amino acids within 4 of the catalytic triad with the 19 other amino acids (column 6, lines 41-47). Thus, according to the teachings of Poulouse, a number of variants would be produced, which would necessarily encompass all position 192, 194, and 219 triple variants, including the specifically recited variants. Because the structure, *i.e.,* amino acid sequence, of a polypeptide determines its function, those polypeptides having the specifically recited substitutions as produced according to Poulouse would necessarily possess the recited increased polyesterase activity. Although Poulouse does not appear to suggest that such variants will have the recited increased polyesterase activity or enhanced thermostability, "the claiming of a...new function or unknown property which is

inherently present in the prior art does not necessarily make the claim patentable." See MPEP 2112. Moreover, while achieving all variants as suggested by Poulouse would require some experimentation, the reference is nonetheless enabling by virtue of disclosing methods of making polypeptide variants.

Conclusion

[14] Status of the claims:

- Claims 1, 39-41, and 45-55 are pending.
- Claims 1, 39-41, and 45-55 are rejected.
- No claim is in condition for allowance.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David J. Steadman whose telephone number is 571-272-0942. The examiner can normally be reached on Mon to Thurs, 7:30 am to 4:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Kathleen Kerr Bragdon can be reached on 571-272-0931. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/David J. Steadman/
David J. Steadman, Ph.D.
Primary Examiner
Art Unit 1656